

**PATENT COOPERATION TREATY**  
**PCT**  
**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**  
(PCT Article 36 and Rule 70)



REC'D 11 FEB 2004

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Applicant's or agent's file reference H1571 PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/04005	International filing date (day/month/year) 16.04.2003	Priority date (day/month/year) 17.04.2002
International Patent Classification (IPC) or both national classification and IPC G01N30/00		
Applicant GENEPROT, INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the opinion
  - II ☐ Priority
  - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV ☐ Lack of unity of invention
  - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☐ Certain defects in the international application
  - VIII ☐ Certain observations on the international application

Date of submission of the demand  07.11.2003	Date of completion of this report  10.02.2004
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Van den Berg, G  Telephone No. +49 89 2399-2499 

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/EP 03/04005**

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17):*

**Description, Pages**

1-13 as originally filed

**Claims, Numbers**

1-21 as originally filed

**Drawings, Sheets**

1/8-8/8 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1 - 21
	No: Claims	none
Inventive step (IS)	Yes: Claims	1 - 21
	No: Claims	none
Industrial applicability (IA)	Yes: Claims	1 - 21
	No: Claims	none

2. Citations and explanations

**see separate sheet**

To point V:

US 6 287 872 B1 (D1) discloses sample support plates for the mass spectrometric analysis of large (bio)molecules including methods for loading the sample support plates with samples of biomolecules from solutions together with matrix substance for the ionisation of the biomolecules using MALDI. In order to allow for automatisisation of the mass spectrometric MALDI analyses of large molecules forming precisely located sample spots with reproducible ionisation yield, the sample support plate is made extremely hydrophobic whereby a favourable structure of MALDI matrix crystals for effective ionisation is generated when driving the sample droplets to sample spots.

US 5 886 345 A (D2), cited in the underlying international application (introductory part on page 2 of the description), describes a method of improving mass resolution by delayed ion acceleration in the field between the sample support and an intermediate electrode wherein added to a test sample an internal reference substance (or ions from the matrix of the MALDI method) may be used as reference ions, in order to compensate for the problem that displacements of the mass scale in regard to the calibration sometimes arise from the fact that the sample layers on the support are of different thicknesses.

1. (Novelty)

Neither document D1 nor D2 discloses all features included in claim 1. Consequently, the subject-matter of claim 1 is novel over the disclosure of either document as is hence the matter included in the dependent claims. Therefore, the subject-matter of claims 1 - 21 meets the requirement of Article 33(2) PCT.

2. (Inventive step)

Document D1 is not concerned with optimising position standards on a target to compensate for offset or drift occurring in measured readings over time and/or distance on the target surface. However, D2 is concerned with that sort of problem (see above) but solves it by applying a correction formula for the flight times of ions from a spectrum scanned

with a faultily adjusted distance  $d$  using a given equation and by then calculating the true masses of the ions from the corrected flight time with the once calibrated mass scale.

Therefore, whereas D1 does not even address the technical problem under consideration, D2 solves that problem via the time of flight route. There is no incentive in document D2 (how) to develop a route to improve the (determination of) of standard positions.

Consequently, the subject-matter of claim 1 is not suggested by this prior art. Nor would a purely hypothetical combination of teachings from documents D1 and D2 reveal the method for positioning mass standards on a MALDI target as claimed in claim 1. As a result, the subject-matter of claim 1 involves an inventive step.

The features in the dependent claims are further advantageous measures for the implementation of the method claimed in claim 1.

Consequently, the subject-matter of claims 1 - 21 meets the requirement of Article 33(3) PCT.

3. (Industrial applicability)

The subject-matter of claims 1 - 21 meets the requirement of Article 33(4) PCT.

Additional remarks:

Possibly, there is a discrepancy between claims and description concerning with regard to features essential to the performance of the invention or not.

Particularly, computing from and application of polynomial transformation to the spectrum of standard-containing positions from the spectrum of the standard-containing position (merely optional in the claims; see claim 17) is expressed as being compulsory in the description (cf. e.g. page 7, lines 15 - 18). This possible inconsistency causes a potential lack of clarity (Article 6 PCT).

In the light of the description, the term "computing the performance of the current  $N$  positions ...." in claim 1 is not clear (cf. e.g. page 9, lines 23 - 32).